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Macro and Micro-Vascular Complications and their Risk Factors in Diabetes Mellitus Patients of Southern Punjab, Pakistan

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Abstract

Background: Diabetes is defined as syndrome and is accompanied by number of micro and macro-vascular complications. The burden is quite high in developing countries so the main aim of this study is to evaluate complications in diabetes patients of Pakistan. **Methods:** A cross-sectional descriptive study was undertaken from December 2015 to March 2016 using a paper based questionnaire. Patients were selected from the 3 private clinics and 3 hospitals employing the systematic sampling technique and anthropometric readings were taken for each individual. The complications were measured by the standards measuring procedures. The demographics were elaborated by the descriptive statistics and the binary logistic regression model was used to analyze the factors associated with the complications by using SPSS version 18. **Results:** Mean age± SD of the respondent's was 48.8±14.6 year. One hundred and thirty (43.5%) were females, 270 (90.3%) were married, 103 (34.5%) were rural resident, 189 (63.2%). Sixty five (21.7%) patients accompany Cardiovascular disease (CVD), 51 (17.0%) had diabetic nephropathy, 96 (32.1) had diabetic neuropathy and 124 (41.5%) had diabetic retinopathy. Age (AOR=2.477 95%CI=1.085, 5.654, p=0.031) and abnormal blood glucose level (AOR=1.872 95%CI=1.005, 3.487, p=0.048) is the significantly affecting factors of CVD. Body mass index was the strongest independent predictor for diabetic nephropathy (AOR=0.233 95%CI=0.067, 0.806, p=0.021) and diabetic retinopathy (AOR=3.558 95%CI=1.884, 6.719 p=0.00). **Conclusion:** The complications seem to be high among the diabetic patients with high frequency of the risk factors accompanying them. Imparting appropriate knowledge and preventing strategies will prove to be of immense benefits in reducing the co-morbidities.

Key words: Micro-Vascular complications, Macro-Vascular complications, Diatbetes, Pakistan.

INTRODUCTION

Diabetes mellitus (DM), by most reasons is a novel disease; exemplary health problem, spreading at an enormous pace and is distressing a large number of population around the globe.[1] In spite of available treatment degenerative effects imparts an enormous social and economic burden.[2] At current the world population suffering from the diabetes is 415 million, which in 2040 is predicted to reach 642 million with the considerable high percentage of type 2 DM.[3] In Pakistan the prevalence of diabetes was found to be 6.9% and is ranked number 6th in the world, which in 2020 will become 4th leading country in the diabetes population.[4-5] This surge in prevalence is credited to distorted lifestyle which is the eventual result of urbanization and socio economic development. Life styles are modernized during the past few decades, resulted from remarkable socioeconomic growth in Pakistan. DM due to its drastic nature and life threatening co-morbidities, is becoming one of leading candidate for morbidity and mortality and is estimated to become 7th leading cause of death by 2030.[6] World Health Organization (WHO) affirmed that DM, in 2012, was responsible for 1.5 million deaths directly and 2.2 million due to high blood glucose.[7]

DM being a syndrome elevates the risk for micro and macro vascular complications. An increase in incidence rate of end stage renal disease (ESRD) due to diabetic nephropathy (DN) was expected correspondingly severe individual and social consequences.[8] Diabetic retinopathy (DR) is the principal cause of blindness in diabetes patients and its cases are mounting gradually.[9] Long term complications of diabetes include peripheral neuropathy (PN) and peripheral vascular disease (PVD). Asymptomatic nature of the PN and PVD is a hurdle in diagnosis and leads to foot ulceration, infection and amputation. However early detection and treatment lessen the prevalence of ulceration.[10] CVD and stroke are rapidly growing macro-vascular complications, strongly associated with the DM and 2-4 folds more common in DM patients than subjects without diabetes. Prevalence of CVD in Eastern Mediterranean region, according to WHO is 26%-36% and accounts for considerable deaths.[11]

In low-middle income country including Pakistan where 70% disease burden is present, patient care in diabetics is imperfect. Despite of high rise in diabetes cases there are few studies which address the DM complications burden on health care system in Pakistan. Prevalence studies of DM related complications give obvious and important information which play a pivotal role in the policy and practice adjustment regarding DM care to gain appropriate control of disease. The past studies indicated the high occurrence of the co-morbidities among diabetics in Pakistan which emphasizes on the strict presentational measures and early detection of diabetes.[12-14]

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The paucity of data in Punjab and other areas demand a need for attention and research activities to estimate the prevalence of co-morbidities in DM patients. In order to establish the regional screening and interventional program it should be noted that what the risk factors for the co-morbidities in Punjab are. As Punjab is the most populace of all the provinces, so it should be focused. Thus, this study aimed to assess the co-morbidities among the diabetes patients and estimation of risk factors for co-morbidities in diabetics.

MATERIAL AND METHODS

Study design: A cross-sectional, study was conducted to collect the data from diabetes patients in southern Punjab, Pakistan from December 2015 to March 2016.

Study site: Site selected for this study was southern Punjab that includes Bahawalpur, Multan and Rahim Yar khan.

Study population and study setting: Patients who were diagnosed with diabetes and were on oral hypoglycemic, insulin or combination therapy regardless of any age, cast, sex, socioeconomic status (SES), religion and were agreed to be the part of study were included in the study. Oral consent was obtained from each and every individual prior to the initiation of the interview. Purposeful request about name contact or any personnel info was not made. Recently diagnosed and patients not willing to participate or could not be able to deal with the investigator (mentally compromised, unconscious) were excluded. Three government health centers and 3 diabetic clinics among the listed ones were chosen. Decision for selection was made on the basis of feasibility for researcher (data collector), more patient flow.

Study sampling: Unavailability of DM registry or any kind of computerized database for diabetes patients in target districts compelled us to adopt systematic random sampling within the selected units (centers/clinics) in order to choose patients to be approached for participation in the study. Thus, every 3rd DM patient was approached. Almost 900 individuals from government hospitals and private clinic were approached, but only 398 individuals responded. Among the approached ones 373 were not interested to take part in the study or were in rush and 129 patients were mentally compromised or gravely ill, were excluded.

Assessment of co-morbidities

Hypertension: Data collectors used mercury sphygmomanometer to evaluate the HTN status of the patients. The definition by WHO for HTN was used in this study.[15]

Diabetic retinopathy: Direct ophthalmoscope method was used to assess the retinopathy after the pupil dilation made by the 1%Tropicamide eye drops. Retinopathy was definite if there was presence of hemorrhage or exudates in either one of the eye or at least one micro aneurysm.

Diabetic Neuropathy: Monofilament, muscle strength and tendon reflex testing were used to estimate the PN. 10 g semmes-weinstein monofilament was used on the foot to estimate the pressure perception. Sensation of site was positive if patient respond yes upon contact of filament. Painful PN was diagnosed if patient had history of pain in body which worsens at night. History of constipation, diahorrea, or postural hypertension was assumed as the determining factor for the autonomic neuropathy (AN).[10]

Nephropathy: Nephropathy was defined as presence of micro or macro albumen and absence of pus cells. Micro albumen was calculated using MICRAL test on ACCU check products. Albumen/ creatinine ratio (ACR) of <30 was termed as normoalbumeneria, 30-300mg/g as microalbuminaria and >300 as macroalbumeneria.[13]

Cardiovascular diseases (CVD): CVD was considered to be present if there was a positive history for chronic heart disease, previous attacks of angina or myocardial Infarction (MI) and was further verified by medical records. While having stroke was exclusively labeled on the basis of patient's history.[13]

Study variable included demographic variable (age, sex, socioeconomic status, education status,) BMI, duration of disease, present medication therapy, family history of diabetes. Body weight was calculated wearing least amount of clothing and height was measured without wearing the shoes. BMI was measured using the standard formula (weight in Kg, divided by the square of the height in m^2). Healthy person falls between a BMI of 18.5 and 24.9. Underweight, overweight, and obesity was considered when BMI was <18.5, 25.0 -29.9 and ≥30.0 respectively. Blood glucose levels (BGL) and total lipid profile (TLP) were measured. Capillary tube whole blood method (using the cholesterol LDX lipid analyzer) was used to measure TLP. If total cholesterol was >5.60 mmol/L dyslipidaemia was taken to be present. Any kind and quantity of cigarette in the previous 12 month were attributed as current smoking.[16]

Statistical analysis: SPSS for Windows, Version 16.0 (SPSS, Chicago, IL, USA) was used for the complete analysis of the data. Demographic variables and co-morbidities were demonstrated by descriptive statistics. Percentages were used for categorical variables whereas continuous variables were articulated by mean ± SD. We employed multivariate regression to identify predictors independently affected the co-morbidities. Cut-off point for p value less than 0.05 was ascribed as existence of statistical significant association. Statistical significance of association among the variables was accessed using 95% CI with a respective odd ratio. Excluded variables for analysis were which contains less than 90% of data.

RESULTS

398 patients with DM were agreed to be the part of the study after approaching 900 patients in 6 different sites adopting systematic random sampling technique. The response rate was 44.3% while data from 299 patients completed the study. Mean age± SD of the respondent's was 48.8±14.6 year and 87 (29.1%) were younger than 40 years of age. One hundred and thirty (43.5%) were females, 29 (9.7%) were single, 103 (34.5%) were rural resident, 189 (63.2%) were under middle school of education and 68 (22.74%) of the study respondents had income below then 15000 PKR. (Table 1)

The mean duration ± SD of diabetes was 9.36 ± 6.9 year. Positive family history of diabetes was found in 204 (68.2%) and 15.3 % of total population was current smoker. 176 (58.8%) were compliant to the exercise and BMI for 60 (20.1%) patients lies in overweight region. Of 299 whose BGL was measured 111 (37.3%) had abnormal BGL and cholesterol level was abnormal in 116 (39.2%) patients. (Table 1)

Among total population, 65 (21.7%) had CVD, s, 51 (17.0%) were suffering from DN. DR was found to be present in 124 (41.5%) patients and 96 (32.1%) were suffering from the diabetic neuropathy (PVD+PN). (Table 2)

Age and BGL after adjusting all the variables significantly associated with the CVD. CVD was likely to be present more than two times in patients aged more than 40 (AOR=2.477 95%CI=1.085, 5.654, p=0.031) and almost twice as likely to be present in patients with the high BGL (AOR=1.872 95%CI=1.005, 3.487, p=0.048). BMI was the strongest independent predictor

Table 1: Demographic characteristics and clinical finding of DM patients.

	Variables	Respondents N (%)
Socio-demographic Characteristics	**Age** 48.8±14.6	
	Less than 40	87 (29.1)
	More than 40	212 (70.9)
	Locality	
	Urban	196 (65.5)
	Rural	103 (34.5)
	Gender	
	Male	169 (56.5)
	Female	130 (43.5)
	Monthly income	
	Less than 15000	68 (22.7)
	More than 15000	231(77.3)
	Marital status	
	Married	270 (90.3)
	Single	29 (9.7)
	Education	
	Up to Middle	189 (63.2)
	More than middle	110 (46.8)
Other baseline variables/ Clinical findings	**Family history of diabetes**	
	Positive	208 (69.6)
	Negative	91 (30.4)
	Duration of diabetes (years) 9.36±6.9	
	Up to 5 years	100 (33.4)
	More than 5 Years	199 (66.6)
	Current treatment	
	Oral Hypoglycemic	158 (52.7)
	Insulin	140 (46.8)
	Total Cholesterol	
	High(>5.60mmol/L)	116 (39.2)
	Normal(≤5.60mmol/L)	180 (60.8)
	BGL	
	Normal	187 (62.7)
	High	111 (37.3)
	BMI	
	Normal	239 (79.9)
	Overweight	60 (20.1)
	Hypertension	
	Yes	133 (44.5)
	No	166 (55.5)
	Smoker	
	Yes	46 (15.38)
	No	253 (84.62)
	Exercise compliance	
	Yes	176 (58.9)
	No	123 (41.1)

Missing values for variables- Current Treatment: 1, Total cholesterol: 3 and BGL: 1.

Table 2: Prevalence of Co-morbidities in DM patients.

Co-morbidity	Number (%)
CVD	65 (21.7)
Diabetic Nephropathy	51 (17.0)
Diabetic Neuropathy	96 (32.1)
Diabetic Retinopathy	124 (41.5)

for DN. Overweight patients were 23.3% likely to have DN than the normal weight individuals (AOR=0.233 95%CI=0.067, 0.806, p=0.021) while all the other factors were insignificantly associated with the DN (P>0.05). Duration of disease and education were the factors which were significantly affecting the diabetic neuropathy. Diabetic neuropathy was almost twice as common in patients with more than 5 years of duration of disease (AOR=1.86 95%CI= 1.009, 3.50 p=0.05). Neuropathy was 54.7% as common in patients with more than middle level of education (AOR= 0.5470 95%CI 0.304, 0.984). BMI was the only variables which was independently associated with the DR. DR was more than three times common in overweight than normal patients (AOR=3.558 95%CI=1.884, 6.719 p=0.00).

DISCUSSION

DM is a syndrome, providing the patients and health care system with great deal of burden in the form of co-morbidities. The data from this study provided a prospective insight for the prevalence of co-morbidities and their risk factors in the DM patients of southern Punjab, Pakistan. Increasing trend in the prevalence of the co-morbidities was observed as compared to the previous studies. Our study indicated that 21.7% of population had CVD, s, 17.0 % had DN, 41.5% had DR and 32.1% had diabetic neuropathy. This prevalence was quite high from previously evaluated prevalence in other parts of Pakistan[12-14] and results were not in line with the studies conducted in Pakistan where the percentage of the co-morbidities was found to be very high in newly diagnosed DM patients. [17] Prevalence of co-morbidities burden is appeared to be far above the ground in the world which corresponds our study.[9- 10,18-20]

In our study risk of having CVD encompasses more than twice in patients over 40 years of age than those less than 40 years of age these results were quite similar with the study conducted in India where the chances of having CVD increase with age[21] whereas the result of pooled analysis predicted the gradient decrease in all forms of CVD over increase in age[22] while in previously conducted study in Pakistan there was no significant association was seen between the age and CVD.[13] BGL is proved to be augmented risk factor for CVD in both type 1 and type 2 DM. Our study indicated that BGL is the independent risk factor for CVD,s. CVD is almost twice as common in patients with abnormal BGL. There were no studies which correlate the high plasma glucose level with CVD subsequent to extensive literature review whereas study conducted in India associate the abnormal HbA1c as the predictor of CHD.[23] Elevated BGL (post parandial) was proved to be the risk factor of CVD with substantial high hazard ratio. [20,22,24] The relation of diabetes with nephropathy is always a point to ponder whereas the diabetes is related with other metabolic disorders as it increases the risk of obesity but in our study only 20.1% of the population was with the overweight or obese stature. In the multivariate analysis BMI is only significant associated factor to nephropathy. There is 77% reduction in chances to have DN with the abnormal BMI (AOR=0.233 95%CI=0.067, 0.806). The significance association was also observed but in otherwise manner in the previous studies.[25] Our study population with duration of disease more than 5 years had significant associated with diabetic neuropathy and neuropathy was almost twice as common as of

Table 3: Multivariate analysis of the associations between selected variables and co-morbidities in diabetes patients.

	Variables	comlicities AOR (95%CI)							
		CVD[a]	P	Diabetic Nephropathy[b]	P	Diabetic Neuropathy[c]	P	Diabetic retinopathy[d]	P
Demographic characters	Age 48.8±14.6								
	Less than 40	1		1		1		1	
	More than 40	2.477 (1.085, 5.654)	0.031	1.11 (0.485, 2.538)	0.80	1.541(0.774, 3.070)	0.218	0.876(0.461, 1.676)	0.695
	Locality								
	Urban	1		1		1		1	
	Rural	1.750 (0.959, 3.193)	0.068	0.936 (0.408, 1.87)	0.85	1.214(0.700, 2.166)	0.491	1.162(0.686, 1.967	0.576
	Gender								
	Male	1		1		1		1	
	Female	1.435(0.766, 2.690)	0.260	1.349 (0.701, 2.791)	0.341	0.845(0.479, 1.489)	0.559	1.256 (0.732, 2.166)	0.404
	Monthly income								
	Less than 15000	1		1		1		1	
	More than 15000	1.060 (0.528, 2.125)	0.87	1.512 (0.949, 2.407)	0.082	0.793(0.428, 1.470)	0.461	1.404 (0.755, 2.609)	0.284
	Marital status								
	Married	1		1		1		1	
	Single	0.930 (0.309, 2.796)	0.89	1.012(0.304, 3.361)	0.986	2.147(0.869, 5.306)	0.09	0.580(0.255, 1.498)	0.260
	Education								
	Up to Middle	1		1		1		1	
	More than middle	1.325(0.707, 2.482)	0.38	0.673 (0.326, 1.388)	0.283	0.547(0.304, 0.984)	0.049	0.826(0.477, 1.433)	0.497
Other baseline variables	Duration of diabetes (years) 9.36±6.9								
	Up to 5 years	1		1		1		1	
	More than 5 Years	0.978 (0.486, 1.970)	0.95	1.773(0.804, 3.90)	0.156	1.860(0.1009, 3.5)	0.044	1.358(0.756, 2.44)	0.306
	Current treatment								
	Oral Hypoglycemic	1		1		1		1	
	Insulin	1.084 (0.581, 2.024)	0.799	1.204 (0.603, 2.408)	0.599	0.747(0.423, 1.319)	0.315	1.146(0.669, 1.963)	0.620
	Total Cholesterol								
	High(>5.60mmol/L)	1.078(0.511, 2.270)		1.672(0.717, 3.899)		1.161(0.595, 2.216)		0.536(0.278, 1.033)	
	Normal(≤5.60mmol/L)	1	0.844	1	0.234	1	0.662	1	
	BGL								
	Normal	1		1		1		1	
	High	1.872 (1.005, 3.487)	0.048	0.599 (0.289, 1.241)	0.168	0.723(0.405, 1.292)	0.274	1.6(0.929, 2.575)	0.062
	BMI								
	Normal	1		1		1		1	
	Overweight	1.097 (0.535, 2.250)	0.80	0.233 (0.067, 0.806)	0.021	0.980(0.497, 1.933)	0.954	3.558(1.884, 6.719)	0.00
	Hypertension	1		1		1		1	
	Yes	0.833 (0.395, 1.757)	0.631	0.834(0.347, 2.007)	0.686	0.932(0.473, 1.853)	0.838	1.67 (0.87, 3.201)	0.122
	No	1		1		1		1	
	Smoker								
	Yes	0.828 (0.395, 1.757)	0.681	1.273 (0.566, 3.202)	0.608	0.652(0.298, 1.456)	0.302	1.041(0.497, 2.181)	0.915
	No	1		1		1		1	
	Exercise compliance								
	Yes	1.017 (0.542, 1.911)	0.975	1.164 (0.573, 2.365)	0.674	0.698(0.399, 1.222)	0.208	1.044(0.723, 2.139)	0.430
	No	1		1		1		1	
Other factor affecting complications									
	Do you repeat ACR test after 3-6 months?								
	Yes			0.354 (0.077, 1.612)	0.179	*		*	
	No			1					
	Do you visit Doctor once in year to test Neuropathy?								
	Yes	*		*		1.077(0.769, 3.232)	0.214	*	
	No					1			
	Do you visit Doctor once in year to test Retinopathy?								
	Yes	*		*		*		1.097(0.699, 2.049)	0.513
	No							1	

*Not available,

[a] Hosmer and Lameshow is 0.757, [b] Hosmer and Lameshow is 0.684

[c] Hosmer and Lameshow is 0.521, [d] Hosmer and Lameshow is 0.668

patients less than 5 years these results were consistent with the previous findings[26-28] whereas these results were contradicted by study in UAE and[10] similarly our results indicated that low level of education is the risk factor and neuropathy is 45.3% less common in patients with more than middle level of education this also coincides with previous results.[10] A significant direct relationship was found between the BMI and DR in our study population where overweight patients had 3.5 times more chances to have DR than underweight. Corresponding results were shown in the previous published data[29] whereas studies from Singapore and India stated an inverse relation between BMI and DR.[30-31]

Poverty and inaccessibility of medicine force the patients to adopt some harsh steps which may prove fatal to them. This is the ultimate failure of the health care system and should be monitored and focused on. Emphasis on improving strategies for management of the disease in low-income and middle-income countries should be of uppermost priority for health care providers.[32] Hence rural, patients of low educational status and socioeconomic status should be motivated via community and health care professionals supports as they are much close to risk factors. This was previously been observed in other parts of world.[33-34] Disease education is the pillar in management of disease and complications also in high and low-middle income countries however the core hurdles in disease management should be evaluated and eradicated.

The main limitations to our study are the non-cooperation of the large number of patients which did not give the true representativeness of the population. The study duration and scale should be enlarged to get the clear prospective of the diabetes and its complications. Genetic and environmental association with the epidemiological date should be performed to determine the effect of ethnic variation and subsequent effect on diabetes management and care.

CONCLUSION

The risk factors and the prevalence of the co-morbidities are substantial in the diabetic patients. Each diabetic patient should be informed and well educated about the risk factors that may lead to development of the complications. The risk factors should be minimized in order to reduce the complications.

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Nil.

CONFLICT OF INTEREST

Nil.

ABBREVIATIONS

Nil.

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